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Mackey-Glass Equation with Variable Coefficients

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Abstract—The Mackey-Glass equation,

$$\frac{dN}{dt} = \frac{r(t)N(g(t))}{1+N(g(t))^\gamma} - b(t)N(t),$$

is considered, with variable coefficients and a nonconstant delay. Under rather natural assumptions all solutions are positive and bounded. Persistence and extinction conditions are presented for this equation. In the case when there exists a constant positive equilibrium, local asymptotic stability of the constant solution and oscillation about this equilibrium are analyzed. The results are illustrated by numerical examples. In particular, it is demonstrated that with delay in both terms, a solution with positive initial conditions may become negative.

Keywords—Delay equations, Extinction and persistence, Mackey-Glass equation, Asymptotics, Oscillation.

1. INTRODUCTION

During the last few decades, it has been recognized that equations with delay more adequately describe various models of mathematical biology than equations without delay. For example, in [1–3], the delay equation (the Mackey-Glass, or the hematopoiesis, equation),

$$\frac{dN}{dt} = \frac{rN_\tau}{1+N_\tau^\gamma} - bN, \tag{1}$$

was applied to model white blood cells production. Here, $N(t)$ is the density of mature cells in blood circulation, the function, $rN_\tau/(1+N_\tau^\gamma)$ modeled the blood cell reproduction, the time lag

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$N_\tau = N(t-\tau)$ described the maturational phase before blood cells are released into circulation, the mortality rate bN was assumed to be proportional to the circulation. Equation (1) was introduced to explain the oscillations in numbers of neutrophils observed in some cases of chronic myelogenous leukemia [1,2].

The reproduction function can differ from one in (1): for instance, $r/(K^\gamma + N^\gamma)$ describes the red blood cells production rate [4], where three parameters r, K, γ are chosen to match the experimental data. This leads to the equation

$$\frac{dN}{dt} = \frac{r}{K^\gamma + N_\tau^\gamma} - bN, \tag{2}$$

it describes the feedback function which saturates at low erythrocite numbers and is a decreasing function of increasing red blood cell levels (i.e., negative feedback).

Various aspects of autonomous equations (1),(2) and some similar models were studied in [5–11]. The main focus was on the existence of periodic solutions, as well as the existence of apparently aperiodic solutions, local and global stability analysis. The summary of some of these results can be found in [12, Sections 4.7–4.9]. Among further developments in this area let us note [13] and recent papers [14–17]. However, in most above-mentioned references autonomous equations were considered (with constant delays and sometimes constant coefficients). In [18], the positiveness of solutions and the global asymptotic stability is studied in some general case, where as an application equation (2) is considered.

In the present paper, we study an equation (1) with variable delay and coefficients,

$$\frac{dN}{dt} = \frac{r(t)N(g(t))}{1 + [N(g(t))]^\gamma} - b(t)N(t), \tag{3}$$

$\gamma > 0$, which in a particular case of constant coefficients r, b and a constant delay $g(t) = t - \tau$ turns into the Mackey-Glass equation. We obtain results on positiveness and boundedness of solutions, on extinction and persistence which extend some results of [12, Sections 4.7–4.9], to equation (1).

The paper is organized as follows. In Section 2, after some preliminaries we prove an auxiliary result on linear delay equations with positive and negative coefficients. Section 3 presents main results of the paper: sufficient conditions for positiveness and boundedness of solutions, extinction, and persistence. In Section 4, we study oscillation of solutions about a positive equilibrium (when it exists) and prove the convergence of any nonoscillatory solution to this equilibrium. In Section 5, we illustrate the sharpness of constraints on coefficients by some numerical simulations and discuss the results.

2. PRELIMINARIES

Consider a scalar delay differential equation,

$$\dot{N}(t) = \frac{r(t)\,N(g(t))}{1 + [N(g(t))]^\gamma} - b(t)\,N(t), \qquad t \ge 0, \tag{4}$$

with the initial function and the initial value,

$$N(t) = \varphi(t), \qquad t < 0, \quad N(0) = N_0, \tag{5}$$

under some of the following conditions:

(a1) $\gamma > 0$;
(a2) $r(t) \ge 0$, $b(t) \ge 0$ are Lebesgue measurable essentially locally bounded functions;
(a3) $g(t)$ is a Lebesgue measurable function, $g(t) \le t$, $\lim_{t\to\infty} g(t) = \infty$;
(a4) $\varphi : (-\infty, 0) \to R$ is a Borel measurable bounded function, $\varphi(t) \ge 0$, $N_0 > 0$;
(a5) $r(t) \ge 0$, $b(t) \ge 0$ are essentially bounded on $[0, \infty)$ functions;
(a6) $\liminf_{t\to\infty} b(t) \ge b > 0$.

DEFINITION. *A locally absolutely continuous function $N : R \to R$ is called a solution of problem (4),(5), if it satisfies equation (4) for almost all $t \in [0, \infty)$ and equalities (5) for $t \le 0$.*

DEFINITION. *We will say that $N(t)$ is an extinct solution of (4),(5) if either*

$$N(t) > 0, \qquad \lim_{t\to\infty} N(t) = 0, \tag{6}$$

or there exists $\bar{t} > 0$ such that $N(t) > 0$, $t < \bar{t}$, $N(\bar{t}) = 0$. A solution of (4),(5) is persistent if it is bounded and

$$\liminf_{t\to\infty} N(t) > 0. \tag{7}$$

We will need the following auxiliary linear equation with positive and negative coefficients,

$$\dot{x}(t) = c(t)\, x(g(t)) - a(t)\, x(t), \tag{8}$$

and the initial conditions,

$$x(t) = \varphi(t) \ge 0, \qquad t < 0, \quad x(0) = x_0 > 0. \tag{9}$$

We also consider the corresponding inequalities,

$$\dot{y}(t) \le c(t) y(g(t)) - a(t) y(t), \tag{10}$$
$$\dot{w}(t) \ge c(t) w(g(t)) - a(t) w(t). \tag{11}$$

LEMMA 1. *Suppose $a(t), c(t)$ are Lebesgue measurable functions, $a(t) \ge 0$, $c(t) \ge 0$, and (a3) holds. Then, the solution of (8),(9) is positive. If $x(t) = y(t) = w(t)$, $t \le t_0$, then $y(t) \le x(t) \le w(t)$, $t \ge t_0$, where $y(t)$ and $w(t)$ are solutions of (10) and (11), respectively.*

Suppose, in addition,

$$\limsup_{t\to\infty} \frac{c(t)}{a(t)} = \lambda < 1, \qquad \int_0^\infty a(s)\, ds = \infty, \tag{12}$$
$$d = \sup_{t<0} \varphi(t) < \infty. \tag{13}$$

Then, for any solution $x(t)$ of (8), we have $\lim_{t\to\infty} x(t) = 0$.

PROOF. Assuming $z(t) = x(t) \exp\{\int_0^t a(s)\, ds\}$, we get

$$\dot{z}(t) = c(t) z(g(t)) \exp\left\{ \int_{g(t)}^t a(s)\, ds \right\},$$

so as far as initial conditions are positive, z is positive and nondecreasing. Since signs of x and z coincide, then x is also positive.

In particular, for fundamental function $X(t,s)$ of equation (8), we have $X(t,s) > 0$, where $X(t,s)$ is the solution of (8) for $t \ge s$ with initial conditions $X(t,s) = 0$, $t < s$; $X(s,s) = 1$.

Denote $u(t) = x(t) - y(t)$, where $y(t)$ is a solution of (10). Then,

$$\dot{u}(t) = c(t)\, u(t) - a(t)\, u(g(t)) + f(t), \qquad u(t) = 0, \quad t \le t_0,$$

where $f(t) \ge 0$. Hence, [19,20]

$$u(t) = \int_{t_0}^t X(t,s)\, f(s)\, ds \ge 0.$$

Since $u(t) = x(t) - y(t)$, then $x(t) \geq y(t)$, $t \geq t_0$. Similarly, if $u(t) = w(t) - x(t)$, where $w(t)$ is a solution of (11), then $u(t) = w(t) - x(t) \geq 0$, which completes the proof of the first statement.

Next, let us prove the second statement of the lemma. Without loss of generality, we can assume $c(t) \leq \lambda a(t)$ for $t \geq 0$.

Denote $A = \max\{d, x(0)\}$, where d is defined in (13). First, let us demonstrate $x(t) \leq A$ for any t.

Otherwise, there exists $\epsilon_0 > 0$ such that $t_0 = \inf_{t>0}\{t \mid x(t) = A + \epsilon_0\} > 0$. Function $x(t)$ is continuous, thus, there exists $t^* < t_0$ such that $\lambda(A + \epsilon_0) < x(t) < A + \epsilon_0$, $t \in [t^*, t_0)$. In this interval $[t^*, t_0)$, the derivative satisfies

$$\dot{x}(t) = c(t)x(g(t)) - a(t)x(t) \leq a(t)[\lambda x(g(t)) - x(t)] \leq 0,$$

which contradicts the assumption $x(t^*) < x(t_0) = A + \epsilon_0$ for $t^* < t_0$. Thus, $x(t) \leq A + \epsilon_0$ for any t. Similarly, we can prove $x(t) \leq A + \epsilon$ for any $\epsilon < \epsilon_0$. Hence, $x(t) \leq A$, for any t. Moreover,

$$\dot{x}(t) = c(t)x(g(t)) - a(t)x(t) \leq [\lambda x(g(t)) - x(t)]a(t) \leq 0,$$

for any t such that $x(t) \geq \lambda A$. Denote $\varepsilon = \lambda + (1 - \lambda)/2$, $\delta = (1 - \lambda)/2$. Since function $x(t)$ is nonincreasing for $x(t) \geq \lambda A$, then there are two possibilities: there exists $t_0 > 0$, such that $x(t) \leq \varepsilon A$ for $t > t_0$ or $x(t) > \varepsilon A$ and it is nonincreasing for any t. Let us demonstrate that the latter case leads to a contradiction: there also exists t_0 such that $x(t) \leq \varepsilon A$ for $t > t_0$. Indeed, if $x(t) \geq \varepsilon A$ for any $t > 0$, then

$$\dot{x}(t) \leq c(t)A - \varepsilon a(t)A \leq \lambda A a(t) - \varepsilon a(t)A = -Aa(t)\frac{1-\lambda}{2} = -A\delta a(t).$$

Since $\int_0^\infty A\delta a(s)\, ds = \infty$, then for some t_0, we have $x(t) < \varepsilon A$.

By (a3) there exists t_1 such that $g(t) > t_0$ for $t > t_1$. Thus, we have a new initial value problem with an initial value $x(t_1)$ and the initial function (which is significant for $t > t_0$ only) not exceeding εA. By applying the same argument, we get

$$\begin{aligned} x(t) &< \varepsilon^2 A, & t &> t_2, & &\text{for some } t_2 > t_1,\\ x(t) &< \varepsilon^3 A, & t &> t_3, & &\text{for some } t_3 > t_2, \dots,\\ x(t) &< \varepsilon^n A, & t &> t_n, & &\text{for some } t_n, \dots. \end{aligned}$$

Since $\varepsilon < 1$, then $\lim_{t\to\infty} x(t) = 0$, which completes the proof.

REMARK. It is easy to see that under the conditions of Lemma 1, the solution is negative for any negative initial conditions.

The case when the second term in the right-hand side of equation (4) involves a delay was considered in [21].

3. POSITIVENESS AND BOUNDEDNESS OF SOLUTIONS

First, let us prove that any solution of (4) is positive.

THEOREM 1. *Suppose (a1)–(a4) hold. Then, any solution of problem (4),(5) is positive for all* $t > 0$.

PROOF. Equation (4) can be rewritten as

$$\dot{N}(t) + b(t)N(t) = \frac{r(t)N(g(t))}{1 + [N(g(t))]^\gamma}, \qquad t \geq 0. \tag{14}$$

Denote

$$N(t) = z(t)\exp\left\{-\int_0^t b(s)\, ds\right\}, \qquad t > 0, \quad z(t) = \varphi(t), \qquad t < 0, \quad z(0) = N(0). \tag{15}$$

Then, (4) takes the form,

$$\dot{z}(t)\exp\left\{-\int_0^t b(s)\,ds\right\} = \frac{r(t)z(g(t))\exp\left\{-\int_0^{g(t)} b(s)\,ds\right\}}{1+z^\gamma(g(t))\exp\left\{-\gamma\int_0^{g(t)} b(s)\,ds\right\}},$$

which can also be rewritten as

$$\dot{z}(t) = \frac{r(t)z(g(t))\exp\left\{\int_{g(t)}^t b(s)\,ds\right\}}{1+z^\gamma(g(t))\exp\left\{-\gamma\int_0^{g(t)} b(s)\,ds\right\}}.$$

Consequently, as far as $\varphi(t) > 0, N(0) = z(0) > 0$, we have $\dot{z}(t) \geq 0$ for any t and z is nondecreasing. Thus, $z(t) > 0$, $t \geq 0$. Since $z(t)$ and $N(t)$ are positive at the same time, then $N(t) > 0$, $t > 0$, which completes the proof.

Now, let us demonstrate that under rather nonrestrictive assumptions any solution of the Mackey-Glass equation is bounded.

THEOREM 2. *Suppose (a1)–(a6) hold and either $\gamma \geq 1$ or*

$$0 < \gamma < 1 \qquad \text{and} \qquad \sup_{t\geq 0}\int_{g(t)}^t b(s)\,ds < \infty.$$

Then, any solution of (4),(5) is bounded for all $t > 0$.

PROOF.

(1) First suppose $\gamma \geq 1$. Then, in the right-hand side of equation (4) the first term does not exceed

$$M = \sup_{t\geq 0} r(t) \sup_{x\geq 0}\frac{x}{1+x^\gamma},$$

where (as straightforward computation gives) the second factor is equal to one, if $\gamma = 1$, and is equal to $(\gamma-1)^{(\gamma-1)/\gamma}/\gamma$, if $\gamma > 1$.

Thus, as far as $N(t) \geq M/b$, where b was defined in (a6), we have $N'(t) < 0$. Consequently, for $t \geq 0$

$$N(t) \leq \max\left\{N_0, \frac{M}{b}\right\} = \begin{cases} \max\left\{N_0, \dfrac{1}{b}\sup_{t\geq 0} r(t)\right\}, & \gamma = 1, \\ \max\left\{N_0, \dfrac{(\gamma-1)^{(\gamma-1)/\gamma}\sup_{t\geq 0} r(t)}{\gamma b}\right\}, & \gamma > 1. \end{cases}$$

(2) Next, let $\gamma < 1$. Since $N'(t) \geq -b(t)N(t)$, then for any t_0, we have

$$N(t) \geq N(t_0)\exp\left\{-\int_{t_0}^t b(s)\,ds\right\}.$$

For instance, assuming $t_0 = g(t)$ yields

$$N(t) \geq N(g(t))\exp\left\{-\int_{g(t)}^t b(s)\,ds\right\} \qquad \text{or} \qquad N(g(t)) \leq N(t)\exp\left\{\int_{g(t)}^t b(s)\,ds\right\}.$$

Since the denominator in the first term of the right-hand side of (4) exceeds $N^\gamma(g(t))$, then

$$\begin{aligned} N'(t) &\leq r(t)N^{1-\gamma}(g(t)) - b(t)N(t) \\ &\leq r(t)N^{1-\gamma}(t)\exp\left\{(1-\gamma)\int_{g(t)}^t b(s)\,ds\right\} - b(t)N(t) \leq AN^{1-\gamma}(t) - bN(t), \end{aligned}$$

where

$$A = \sup_{t \geq 0} \left[r(t) \exp\left\{ (1-\gamma) \int_{g(t)}^{t} b(s)\, ds \right\} \right].$$

Thus, the solution of (4) does not exceed the solution of the Bernoulli equation

$$y'(t) + by = Ay^{1-\gamma}, \tag{16}$$

with the same initial condition. Since the general solution of (16) is

$$y(t) = \left(\frac{A}{b} + Ce^{-\gamma b t} \right)^{1/\gamma},$$

then any solution of (16) is bounded. Thus, any solution of (4) is also bounded, which completes the proof.

Let us proceed to persistence conditions.

First, we obtain an auxiliary result on the nonlinear function,

$$f(x) = \frac{\lambda x}{1 + x^{\gamma}}. \tag{17}$$

Obviously, $f(0) = 0$ and the function f has the only positive equilibrium point,

$$N^* = (\lambda - 1)^{1/\gamma}. \tag{18}$$

LEMMA 2. *For any $\gamma > 0$ $f(x)$ defined by (17) is a continuous function satisfying*

$$f(x) > x, \qquad 0 < x < N^*, \quad f(x) < x, \qquad x > N^*, \tag{19}$$

where N^* is as in (18). If $0 < \gamma < 1$, then f is increasing.

For any $M > N^*$ there exists m, $0 < m < N^*$, such that for any m_1, $m \geq m_1 > 0$, the inequality $M \geq x \geq m_1$ implies $f(x) \geq m_1$.

PROOF. Since the derivative of f

$$f'(x) = \left(\frac{\lambda x}{1 + x^{\gamma}} \right)' = \lambda \frac{(1-\gamma)x^{\gamma} + 1}{(1 + x^{\gamma})^2} \tag{20}$$

is positive for $0 < \gamma < 1$, then f is increasing. For any $\gamma > 0$, we have $f(0) = 0$, $\lim_{t \to \infty} [f(x) - x] = -\infty$, so the continuous function $f(x) - x$ keeps its sign between two zeros at 0 and N^* and after N^*. Thus, (19) is valid. If $0 < \gamma < 1$, then f is increasing (see also Figure 1).

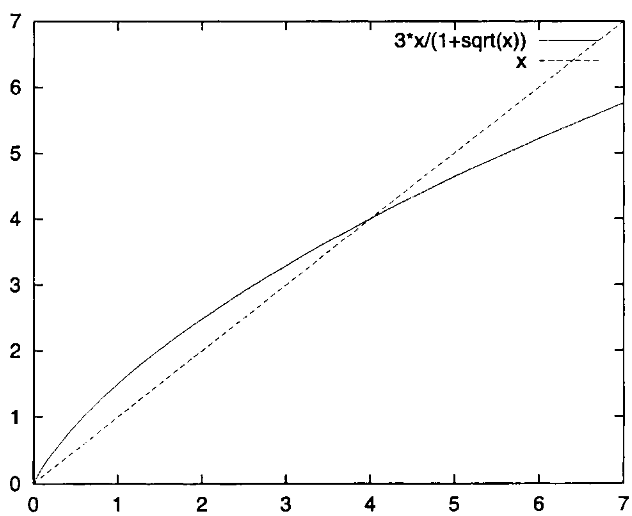

Figure 1. The graph of $f(x) = \lambda x/(1 + x^{\gamma})$ for $\lambda = 3$, $\gamma = 0.5$. Here, $f(x)$ is increasing and for any $m_1 < N^*$, where N^* is the equilibrium point, $x > m_1$ implies $f(x) > f(m_1) > m_1$.

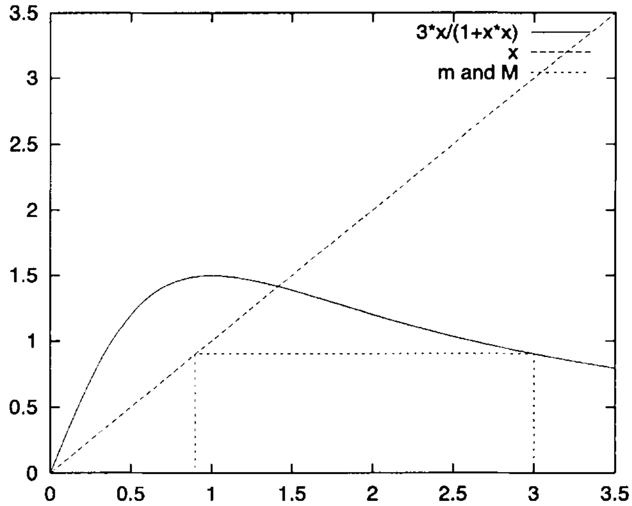

Figure 2. The graph of $f(x) = \lambda x/(1+x^\gamma)$ for $\lambda = 3$, $\gamma = 2$. For example, if $x < M = 3$, then for any $m_1 < m = 0.9$ the inequality $x > m_1$ implies $f(x) > m_1$.

Next, let us show that for some $m > 0$ the estimate $x \geq m$ implies

$$f(x) = \frac{\lambda x}{1+x^\gamma} \geq m. \tag{21}$$

If $0 < \gamma \leq 1$, then f is nondecreasing and for any N satisfying $N(t) \geq m = N^*$ the estimate (21) holds. Moreover, if $m_1 < m = N^*$, then $x > m_1$ implies $f(x) > f(m_1) > m_1$.

Now let $\gamma > 1$ (see Figure 2). Then, generally speaking, there is no such m that the estimate (21) is correct for any $x > m$ since $\lim_{x\to\infty} f(x) = 0$. However, we have assumed $x < M$.

We assumed $M > N^*$, then denote

$$m = \min_{N^* \leq x \leq M} f(x) > 0.$$

We have $f(x) > x$ for $0 < x < N^*$. By the definition of m for any $m_1 \leq m$, $x > m_1$, we have $f(x) \geq m \geq m_1$ for $M \geq x \geq N^*$; if $m_1 \leq x < N^*$, then $f(x) > x \geq m_1$.

Thus, we found such $m > 0$, $N^* \geq m > 0$ that (19) holds, which completes the proof of the lemma.

REMARK. If $M \leq N^*$, we can denote $m = M$. Then, for any $m_1 < m$, the inequality $x \geq m_1$ implies $f(x) > x > m_1$, since $x < N^*$. Thus, (19) holds.

THEOREM 3.

(1) *Suppose (a1)–(a4) hold and*

$$\inf_{t<0} \varphi(t) > 0, \qquad N_0 > 0, \qquad \liminf_{t\geq 0} \frac{r(t)}{b(t)} = \lambda > 1. \tag{22}$$

Then, any bounded solution of (4),(5) is persistent.

(2) *Suppose (a1)–(a6) and (22) hold and either $\gamma \geq 1$ or*

$$0 < \gamma < 1 \qquad \text{and} \qquad \sup_{t\geq 0} \int_{g(t)}^{t} b(s)\, ds < \infty. \tag{23}$$

Then, any solution of (4),(5) is persistent.

PROOF. Without loss of generality, we can assume $\inf_{t\geq 0} r(t)/b(t) = \lambda > 1$.

By the hypothesis of the Theorem, the solution is bounded $N(t) < M$, we can assume $M > N^*$. For a given M, let us find m, $N^* \geq m > 0$ as in Lemma 2, such that for every $0 < m_1 \leq m$ the inequality $M \geq x \geq m_1$ implies $f(x) \geq m_1$, where $f(x)$ is defined in (17).

Denote $A = \min\{N_0, \inf_{t<0} \varphi(t), m\}$ and demonstrate $N(t) \geq A$ for any t. Let us note that A is a lower bound of the function $f(x)$ when $x \geq m$, since $f(x) \geq m \geq A$ for $x \geq m$.

Assuming $N(t) < A$ for some t, we get a nonempty set (N is a continuous function)

$$S = \{t \geq 0 \mid N(t) = A, N(s) < A,\ s \in (t, t+\varepsilon),\ \text{for some } \varepsilon > 0\}.$$

Consider $t_1 = \inf S \geq 0$. Then $N(t_1) = A, N(t) \geq A$, $t < t_1$, and for some $\varepsilon > 0$, we have $N(t) < A$, $t \in (t_1, t_1+\varepsilon)$.

Since $A \leq m \leq N^*$, we can assume $A < N^*$. In the case $A = N^*$, we can present the proof for any lower bound $A - \delta < N^*$ which will lead to the conclusion: A is a lower bound for the solution.

Since $f(x)$ is a continuous function and $f(x) > x$ for $x < N^*$, then there exists $\tau > 0$ small enough, such that $f(A-\tau) \geq A$ and $f(x) > A$ for $x \in (A-\tau, A)$. $N(t)$ is a continuous function, $N(t_1) = A$, $N(t) < A$, when $t \in (t_1, t_1+\varepsilon)$. Let us take $\varepsilon > 0$ small enough, such that $A - \tau < N(t) < A$ for $t \in (t_1, t_1+\varepsilon)$. Then, for any $t < t_1 + \varepsilon$ we have $f(N(g(t))) > A$. Indeed, if $g(t) > t_1$, then $A - \tau < x = N(g(t)) < A$, hence, $f(x) > A$. If $g(t) < t_1$, then by definition of A, we have $N(g(t)) > A$. Hence, Lemma 2 implies $f(N(g(t))) > A$.

For $t \in (t_1, t_1+\varepsilon)$, we have

$$\begin{aligned} N(t) &= N(t_1) + \int_{t_1}^{t} \left[\frac{r(s)N(g(s))}{1+[N(g(s))]^\gamma} - b(s)N(s)\right] ds \\ &\geq A + \int_{t_1}^{t} b(s)\left[\frac{\lambda N(g(s))}{1+[N(g(s))]^\gamma} - A\right] ds \\ &\geq A + \int_{t_1}^{t} b(s)[A - A] = A, \end{aligned}$$

which contradicts the assumption: $N(t) < A$, $t \in (t_1, t_1+\varepsilon)$. Thus, $N(t) \geq A$ for any t.

The reference to Theorem 2 completes Part (2).

REMARK. For the case $0 < \gamma < 1$, in Theorem 3, we have proved a stronger claim: if the initial function and value do not exceed N^*, then the lower bound of the solution will not go beyond the infimum of its prehistory. Lemma 9.1 [12, p. 158–159] presents a similar result for constant coefficients and a constant delay (where N^* is the positive equilibrium point).

We proceed to extinction conditions.

THEOREM 4. *Suppose (a1)–(a4) hold and*

$$\limsup_{t\to\infty} \frac{r(t)}{b(t)} = \lambda < 1, \qquad \int_0^\infty b(s)\, ds = \infty, \qquad \sup_{t<0} N(t) < \infty.$$

Then, the solution $N(t)$ of (4),(5) tends to zero $\lim_{t\to\infty} N(t) = 0$.

PROOF. Since any solution is positive, then we have

$$\dot N(t) \leq r(t)N(g(t)) - b(t)N(t).$$

Thus, the reference to Lemma 1 completes the proof.

REMARK. In the case of an autonomous equation, Theorem 4 implies a well known result [12] on global attractivity of the zero solution.

4. ASYMPTOTICS AND OSCILLATION

Let us consider an equation of type (4) which has a constant positive equilibrium,

$$\dot{N}(t) = r(t)\left[\frac{aN(g(t))}{1+[N(g(t))]^{\gamma}} - bN(t)\right], \tag{23}$$

with the initial conditions (5) under the following assumptions,

(b1) $\gamma > 0$;
(b2) $r(t) \geq 0$ is a Lebesgue measurable essentially locally bounded function, $b > 0$, $a > b > 0$;
(b3) $g(t)$ is a Lebesgue measurable function, $g(t) \leq t$, $\limsup_{t\to\infty}(t - g(t)) < \infty$;
(b4) $\varphi : (-\infty, 0) \to R$ is a Borel measurable bounded function, $\varphi(t) \geq 0$, $N_0 > 0$;
(b5) $\liminf_{t\to\infty} r(t) > 0$.

The equation has a constant equilibrium,

$$N^* = \left(\frac{a}{b} - 1\right)^{1/\gamma}. \tag{24}$$

We also consider the linear equation,

$$\dot{x}(t) = r(t)\left[\frac{a}{1+(N^*)^{\gamma}}x(g(t)) - bx(t)\right], \tag{25}$$

which is a partial case of (8), with the shifted initial conditions,

$$x(t) = \zeta(t) = \varphi(t) - N^*, \qquad t < 0, \quad x(0) = x_0 = N(0) - N^* = N_0 - N^*, \tag{26}$$

DEFINITION. *We will say that the solution of (25),(26) oscillates if it is neither eventually positive nor eventually negative for $t > 0$. The solution of (23),(5) oscillates about N^* if $N - N^*$ is neither eventually positive nor eventually negative for $t > 0$.*

DEFINITION. *We will say that the equilibrium solution $N = N^*$ of equation (23) is (locally) stable, if for any $\epsilon > 0$, there exists $\delta > 0$ such that for every initial conditions $|N(0) - N^*| < \delta_0$, $|\varphi(t) - N^*| < \delta_0$, $\delta_0 \leq \delta$, for the solution $N(t)$ of (23),(5), we have $|N(t) - N^*| < \epsilon$, $t \geq 0$.*

If, in addition, $\lim_{t\to\infty} N(t) = N^*$, then the solution $N = N^*$ of equation (23) is locally asymptotically stable.

We will use the same definition for the locally asymptotically stable zero solution of (25) with the corresponding shifted initial conditions (26).

Consider the following restriction on the exponent γ,

$$\gamma < \frac{a}{a-b}. \tag{27}$$

The following lemma demonstrates that (27) is a sufficient condition for the local asymptotic stability of equation (23).

THEOREM 5. *Suppose Hypotheses (b1)–(b5) hold together with one the following inequalities,*

$$\gamma < \frac{a}{a-b} \qquad \text{or} \qquad \frac{a}{a-b} < \gamma < \frac{2a}{a-b}. \tag{28}$$

Then, the equilibrium solution $N = N^*$ of equation (23) is locally asymptotically stable.

PROOF. The statement of the theorem is a corollary of the following result [22, Theorem 6, Part 1].

Suppose (b1)–(b5) hold (with the restrictions valid for both delays g and h) and

$$\limsup_{t\to\infty} \int_{h(t)}^{t} r(s)\,ds < \frac{a - |\gamma(a-b) - a|}{(a + |\gamma(a-b) - a|)b}. \tag{29}$$

Then, for the equation,

$$\dot N(t) = r(t)\left[\frac{aN(g(t))}{1 + [N(g(t))]^{\gamma}} - bN(h(t))\right], \qquad t \ge 0, \tag{30}$$

the positive steady state N^* defined by (24) is locally asymptotically stable.

Assuming $h(t) \equiv t$ we obtain that (29) is equivalent $a > |\gamma(a-b) - a|$ (since $a, b > 0$). Taking into account (28), we have

$$|\gamma(a-b) - a| = \begin{cases} a - \gamma(a-b), & \gamma < \dfrac{a}{a-b}, \\ \gamma(a-b) - a, & \dfrac{a}{a-b} < \gamma < \dfrac{2a}{a-b}, \end{cases}$$

thus, (29) becomes $a > a - \gamma(a-b)$, or $\gamma(a-b) > 0$, in the first case, which is obvious in view of (b1)–(b2). In the latter case, (29) turns into $a > \gamma(a-b) - a$, or $a < \gamma(a-b) < 2a$, which is equivalent to the second condition in (28).

Thus, (28) is a sufficient condition of local asymptotic stability of the positive equilibrium N^* for equation (23), which completes the proof.

THEOREM 6. *Suppose hypotheses (b1)–(b5) hold. If a solution of (25) with initial conditions (26) oscillates, then a solution of equation (23) with the initial condition (5) also oscillates about N^*.*

If equation (23) has a nonoscillatory about N^* solution then it tends to the positive equilibrium,

$$\lim_{t\to\infty} N(t) = N^*.$$

PROOF. Let us assume equation (23) has a nonoscillatory about N^* solution. Making a substitution $y = N - N^*$, we provide that the solution of the equation

$$\dot y(t) = r(t)\left[\frac{a[y(g(t)) + N^*]}{1 + (y(g(t)) + N^*)^{\gamma}} - by(t) - bN^*\right] \tag{31}$$

is oscillatory if and only if the solution of (23) is oscillatory about N^*. If (23) has a nonoscillatory about N^* solution, then there exists either positive or negative solution of (31). Then, without loss of generality, we can assume equation (23) has a solution, $y(t) > 0$, $t > 0$. Then,

$$\begin{aligned}
\dot y(t) &= r(t)\left[\frac{a[y(g(t)) + N^*]}{1 + (y(g(t)) + N^*)^{\gamma}} - by(t) - bN^*\right] \\
&\le r(t)\left[\frac{a[y(g(t)) + N^*]}{1 + (N^*)^{\gamma}} - by(t) - bN^*\right] \\
&= r(t)\left[\frac{a}{1 + (N^*)^{\gamma}}y(g(t)) + \frac{aN^*}{1 + (N^*)^{\gamma}} - bN^* - by(t)\right] \\
&= r(t)\left[\frac{a}{1 + (N^*)^{\gamma}}y(g(t)) - by(t)\right].
\end{aligned}$$

By Lemma 1, equation (25) with initial conditions (26) has a positive solution $x(t) \ge y(t) > 0$ since the corresponding inequality has a positive solution. We have a contradiction which proves the first part of the theorem for this case.

Under Hypotheses (b1)–(b5), conditions (12),(13) of Lemma 1 are satisfied. Thus,

$$\lim_{t\to\infty} x(t) = 0,$$

which implies $\lim_{t\to\infty} y(t) = 0$ and $\lim_{t\to\infty} N(t) = N^*$.

Similarly, if we assume $y(t) < 0$, $t > 0$, then we obtain

$$\dot{y}(t) \geq r(t)\left[\frac{a}{1+(N^*)^\gamma} y(g(t)) - by(t)\right],$$

which by Lemma 1 yields equation (25) has a negative solution $x(t) \leq y(t)$. Again, by Lemma 1 $\lim_{t\to\infty} x(t) = 0$ implies $\lim_{t\to\infty} N(t) = N^*$.

REMARK. By Lemma 1, the solution of equation (25) is nonoscillatory if the initial function is nonoscillatory. Thus, it is natural to expect that a solution of (23) oscillates about the positive equilibrium N^* when the initial function oscillates about N^*. This is confirmed by numerical simulations for the case of a constant delay and constant $r(t)$ (see, for example, [2]).

THEOREM 7. *Suppose (b1)–(b5) and (27) hold. Then, there exist such initial conditions (5) that the solution of equation (23) is nonoscillatory about N^*.*

PROOF. Consider the following function,

$$\alpha(y) = (1+(N^*)^\gamma)\left[\frac{a(y+N^*)}{1+(y+N^*)^\gamma} - bN^*\right]. \tag{32}$$

By (24) $\alpha(0) = 0$, besides,

$$\alpha'(y) = \frac{a(1+(N^*)^\gamma}{(1+(y+N^*)^\gamma)^2}\left[1+(y+N^*)^\gamma - \gamma(y+N^*)^\gamma\right].$$

Thus, the derivative at $y = 0$ equals

$$\begin{aligned}\alpha'(0) &= \frac{a}{1+(N^*)^\gamma}\left[1+(N^*)^\gamma - \gamma(N^*)^\gamma\right]\\ &= \frac{a}{a/b}\left[\frac{a}{b} - \gamma\left(\frac{a}{b}-1\right)\right]\\ &= b\left[\frac{a}{b} - \gamma\frac{a-b}{b}\right] = a - \gamma(a-b).\end{aligned}$$

Consequently, if (27) holds then $\alpha'(0) = a - \gamma(a-b) > 0$.

Let us take a positive τ, $0 < \tau < \alpha'(0)$. Then, there exists $\varepsilon > 0$, such that $|y| < \varepsilon$ implies $\alpha(y) \geq \tau y$, which is equivalent to

$$\frac{a(y+N^*)}{1+(y+N^*)^\gamma} - bN^* \geq \frac{\tau y}{1+(N^*)^\gamma}.$$

Thus, as far as solution $y(t)$ of equation (31) satisfies $|y(t)| < \varepsilon$ for any t, by Lemma 1, this solution is not less than the solution of the linear equation,

$$\dot{x}(t) = r(t)\left[\frac{\tau x(g(t))}{1+(N^*)^\gamma} - bx(t)\right], \tag{33}$$

which is positive by Lemma 1 for any positive initial conditions.

On the other hand, by Theorem 5 $y = 0$ in (31) is locally asymptotically stable. This means that for any $\varepsilon > 0$ there exists $\delta > 0$, such that $\max\{|y(0)|, \sup_{t<0}|y(t)|\} < \delta$ implies $|y(t)| < \varepsilon$ for any t. Let us assume positive initial conditions not exceeding δ. Then, $y(t) \geq x(t)$, where x is a positive solution of (33). Hence, y is nonoscillatory and $N(t) > N^*$ for the corresponding initial conditions, which completes the proof.

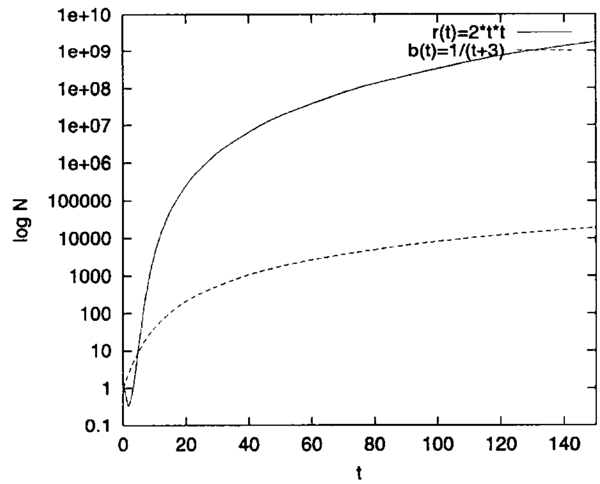

Figure 3. The solutions of (34) and (35) are unbounded, where either (a5) or (a6) does not hold. In (34), $r(t) = 2t^2$ is not bounded for $t > 0$, while in (35) for $b(t) = 1/(t+3)$ the condition (a6) is not satisfied. In both simulations $N(0) = 1, \varphi(t) \equiv 1$. We use the logarithmic scale for $N(t)$.

5. EXAMPLES AND DISCUSSION

Theorems 1 and 2 illustrate that for the variable Mackey-Glass equation under rather natural constraints on coefficients the model is "well posed" in the following sense.

(1) N cannot become zero or negative.
(2) N is globally bounded.

Really, in the original biomedical model the amount of white blood cells is positive and bounded which should be reflected in the model even if production and mortality rates can vary.

Example 1 demonstrates that the global boundedness of $r(t)$, as well as $b(t) \geq b > 0$, are crucial for the boundedness of a solution.

EXAMPLE 1. Let us demonstrate that with (a5),(a6) omitted in Theorem 2, the solution can be unbounded. For instance, consider two equations,

$$\dot{N}(t) - \frac{2t^2 N(t)}{1+\sqrt{N(t)}} + N(t) = 0, \tag{34}$$

$$\dot{N}(t) - \frac{2N(t)}{1+\sqrt{N(t)}} + \frac{N(t)}{t+3} = 0. \tag{35}$$

In (34), $r(t) = 2t^2$ is not bounded for $t > 0$, while in (35) for $b(t) = 1/(t+3)$, Condition (a6) is not satisfied since $\lim_{t\to\infty} b(t) = 0$. Solutions of (34),(35) in the logarithmic scale are presented in Figure 3.

Theorems 3 and 4 present sufficient conditions for extinction and persistence of solutions. Let us illustrate the fact that the equality $\int_0^\infty b(t)dt = \infty$ is required in Theorem 4 to deduce extinction of solutions.

EXAMPLE 2. The equation

$$\dot{N}(t) - \frac{2e^{-t}N(t)}{1+\sqrt{N(t)}} + 2.1e^{-t}N(t) = 0, \tag{36}$$

has a persistent solution (see Figure 4, where $N(t) \approx 2.817214$, $t > 16$); here, $\int_0^\infty b(t)\,dt = \infty$ is not satisfied. We can easily see that other conditions of Theorem 4 are satisfied, with $\lambda = 2/2.1 < 1$.

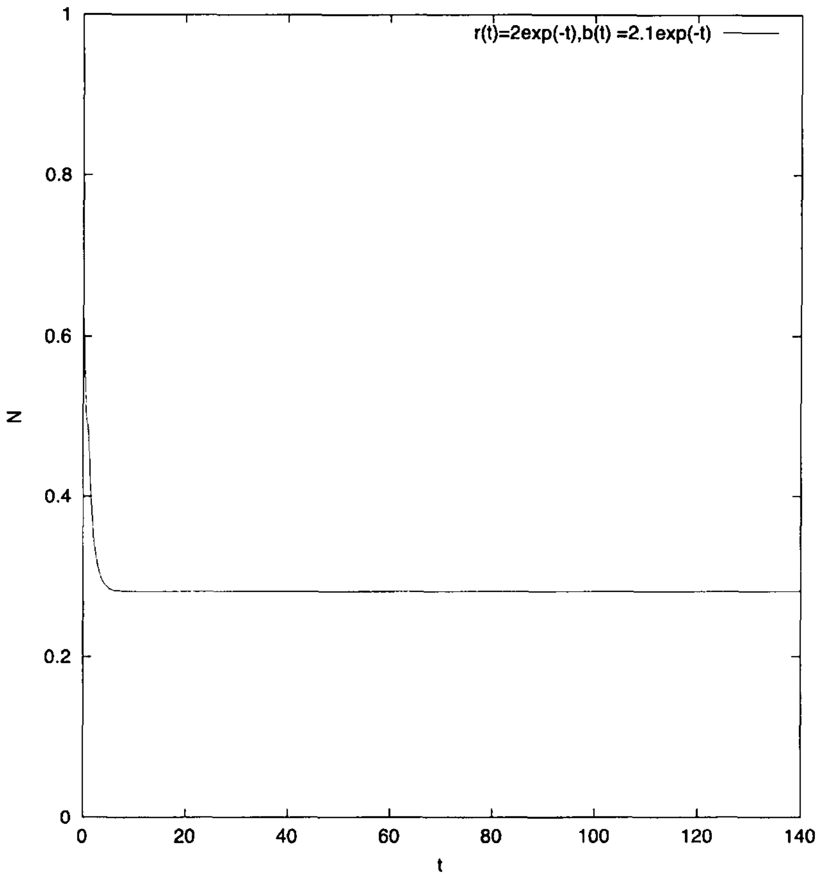

Figure 4. The solution of (36) does not tend to zero. Here, $b(t) = 2.1e^{-t}$ not only does not satisfy $b(t) \geq b > 0$, but even its integral at infinity converges.

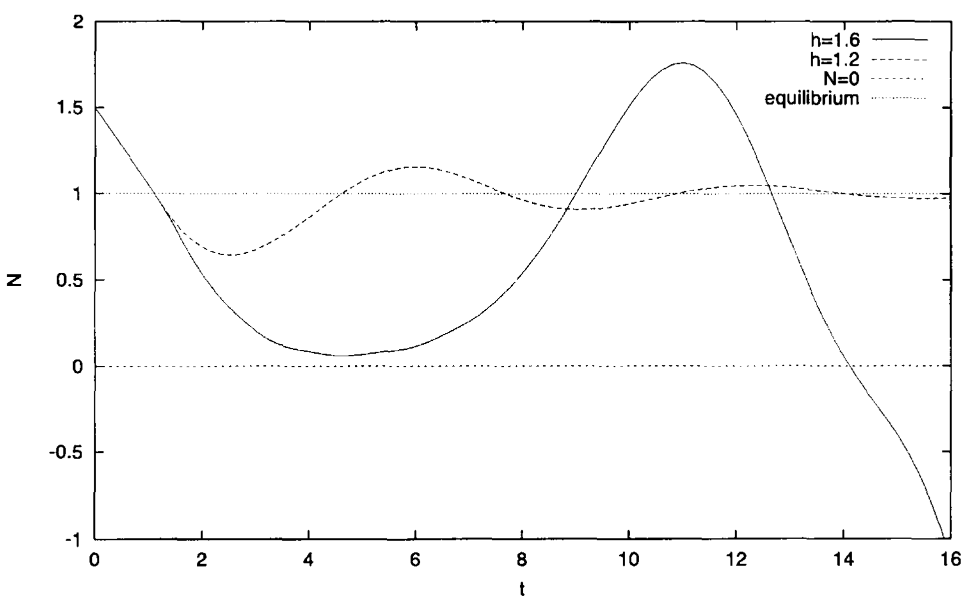

Figure 5. The solution of (38), with $N(0) = 1.5$, $\varphi(t) \equiv 1.5$, $r = 3$, $b = 1.5$, $g = 1$, $h = 1.6$ becomes negative, while for a smaller delay $h = 1.2$ the solution is positive.

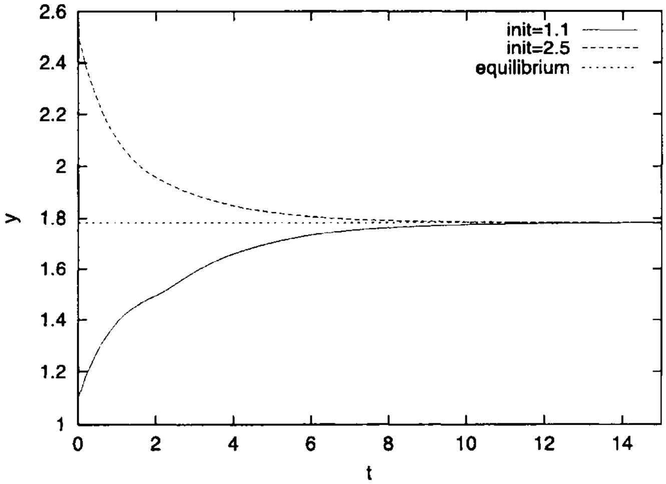

Figure 6. The solution of (39), with $a = 3$, $b = 1$, $c = 1.2$, $g = 2$, initial conditions $N(0) = 1.1$, $\varphi(t) \equiv 1.5$ and $N(0) = 2.5, \varphi(t) \equiv 2.5$, respectively. Here, $c = 1.2 < a/(a-b) = 1.5$, so the nonoscillation condition (27) is satisfied.

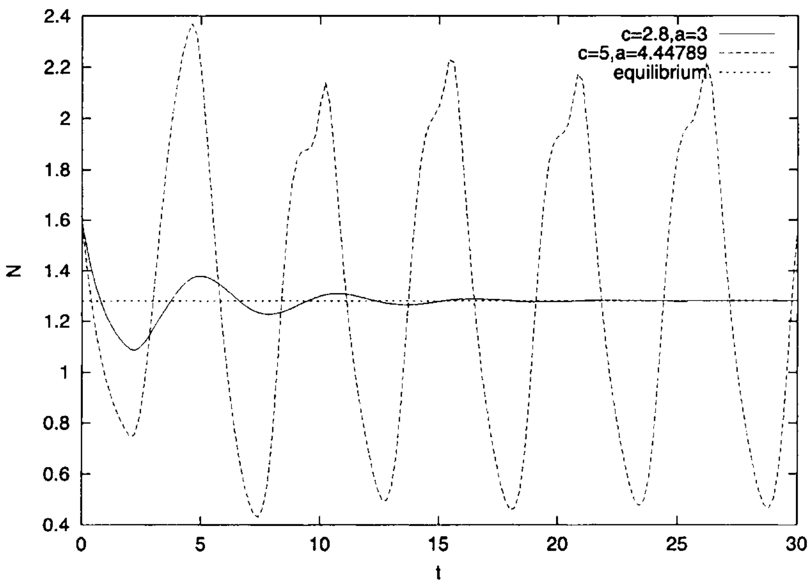

Figure 7. The solution of (39), with $b = 1$, $g = 2$, initial conditions $N(0) = 1.6$, $\varphi(t) \equiv 1.6$, $a = 3$, $c = 2.8$, and $a \approx 4.44789$, $c = 5$, respectively. In the first case, $a/(a-b) < c < 2a/(a-b)$, the solution oscillates and tends to the equilibrium, while in the latter case $c > 2a/(a-b)$, the solution oscillates and does not tend to the equilibrium.

Let us consider a certain generalization of (4) with a possibility of the delay in the mortality term

$$\dot{N}(t) = \frac{r(t)N(g(t))}{1 + N(g(t))^{\gamma}} - b(t)N(h(t)), \qquad t \geq 0. \tag{37}$$

We do not know how to extend our results to this case. To the best of our knowledge, there are no results for (37) even in the autonomous case. However, the following numerical simulation shows that the properties of this equation are quite different; for example, it can assume negative solutions. The result is not quite unexpected: it is well known that, unlike the logistic equation with one delay, the solution of a logistic equation with two delays can become negative [23].

EXAMPLE 3. Let us consider the following equation with two delays,

$$\dot{N}(t) - \frac{rN(t-g)}{1+N(t-g)} + bN(t-h) = 0. \tag{38}$$

Figure 5 demonstrates that the solution for $r = 3$, $b = 1.5$, $g = 1$, $h = 1.6$, $\varphi(t) \equiv N(0) = 1.5$ becomes negative, while for a smaller delay $h = 1.2$ the solution is positive (and tends to the equilibrium $N = 1$ as $t \to \infty$). For some more detailed discussion on (3) with delay in the harvesting term and with a nondelayed production term, see [21].

EXAMPLE 4. Finally, let us illustrate results on asymptotics and oscillation of solutions. To this end, let us consider equation (23) with constant parameters and constant initial function,

$$\dot{N}(t) = \frac{aN(t-g)}{1+(N(t-g))^c} - bN(t), \quad N(t) = \varphi(t) \equiv N(0), \qquad t < 0. \tag{39}$$

First, let us assume c is in nonoscillation domain $c < a/(a-b)$. Figure 6 demonstrates two nonoscillating solutions for $a = 3$, $b = 1$, $c = 1.2$, $g = 2$, with the initial conditions $\varphi(t) \equiv N(0) = 1.1$ and 2.5, respectively.

Further, let us proceed to the oscillation domains $a/(a-b) < c < 2a/(a-b)$ (the solution is expected to tend to the equilibrium) and $c > 2a/(a-b)$ (the solution is not expected to tend to the equilibrium). Figure 7 illustrates two cases, in both $b = 1$, $g = 2$, $N(0) = 1.6, \varphi(t) \equiv 1.6$. In the first case $a = 3$, $c = 2.8$, $a/(a-b) = 1.5 < c$, and $2a/(a-b) = 3 > c$, the solution oscillates and tends to the equilibrium. In the second case, $a \approx 4.44789$, $c = 5$, (we have the same equilibrium $N^* \approx 1.28$ in both cases), we have $c = 5 > 2a/(a-b)$; the solution oscillates and does not tend to the equilibrium value.

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